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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,710	02/24/2004	Mark L. Nelson	16534-512C01US	3651
30623	7590	03/24/2010	EXAMINER	
MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C.			HAVLIN, ROBERT H	
ONE FINANCIAL CENTER			ART UNIT	PAPER NUMBER
BOSTON, MA 02111			1626	
MAIL DATE		DELIVERY MODE		
03/24/2010		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>		<b>Application No.</b>	<b>Applicant(s)</b>
10/786,710		NELSON ET AL.	
<b>Examiner</b>	<b>Art Unit</b>		
ROBERT HAVLIN	1626		

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### **Status**

1) Responsive to communication(s) filed on 08 March 2010.  
 2a) This action is FINAL.      2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### **Disposition of Claims**

4) Claim(s) See Continuation Sheet is/are pending in the application.  
 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1,4,6,7,9-11,13,19,21,23,24 and 82 is/are rejected.  
 7) Claim(s) 32,103,109 and 110 is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### **Application Papers**

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### **Priority under 35 U.S.C. § 119**

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### **Attachment(s)**

1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement(s) (PTO/SB/08)  
 Paper No(s)/Mail Date \_\_\_\_\_

4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date \_\_\_\_\_

5) Notice of Informal Patent Application  
 6) Other: \_\_\_\_\_

Continuation of Disposition of Claims: Claims pending in the application are 1, 4, 6-7, 9-11, 13, 14, 19, 21, 23-26, 30, 32, 34-40, 56-65, 67, 68, 82, 103-112, 117-143, 145-147, and 149-158.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 14,25,26,30,34-40,56-65,67,68,104-108,111,112,117-143,145-147 and 149-158.

**DETAILED ACTION**

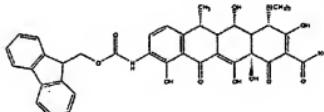
**RCE:** A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/8/10 has been entered.

**Status of the claims:** Claims 1, 4, 6-7, 9-11, 13, 14, 19, 21, 23-26, 30, 32, 34-40, 56-65, 67, 68, 82 and 103-112, 117-143, 145-147, and 149-158 are pending in the application.

***Election / Restriction***

Applicant previously elected Group I drawn to products of Formula I as acknowledged in the office action of 1/5/2006:

Acknowledgement is made of Applicant's election (without traverse) of Group I and, for search purposes, the species,



, in a response filed 11/09/2005.

Claims 1, 4, 6-7, 9-11, 13, 19, 21, 23-24, 32, 82, 103, 109, and 110 read on the elected species.

As detailed in the following rejections, the generic claim encompassing the elected species was not found patentable. Therefore, the provisional election of species is given effect, the examination is restricted to the elected species only, and

claims not reading on the elected species are held withdrawn. Accordingly, claims 14, 25, 26, 30, 34-40, 56-65, 67, 68, 104-108, 111, 112, 117-143, 145-147, and 149-158 not reading on the elected species are withdrawn from consideration.

Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection through amendment, the amended Markush-type claim will be reexamined to the extent necessary to determine patentability of the Markush-type claim. See MPEP 803.02.

**RESPONSE TO APPLICANT REMARKS**

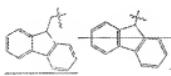
***Claim Rejections - 35 USC § 103***

1. Claims 1, 7, 11, 23-25, and 67 were rejected under 35 U.S.C. 103(a) as being unpatentable over Barden et al. (J. Med Chem, 1994, v. 37, no. 20, p. 3205-3211) in view of Silverman, R. B. (The Org. Chem. of Drug Design and Drug Action, Academic Press, Inc.: San Diego, 1992, pp. 4-51).

Applicant has amended the claims to delete the alternatives of lower alkyl from R9a in the claims. Thus, the claims now require that any alkyl at the R9a position be substituted. This constitutes a non-obvious difference between the prior art and the claims. Accordingly, this rejection is **withdrawn**.

***Claim Rejections - 35 USC § 112***

2. The amended claim 32 was previously rejected as creating an unsupported new

subgenus with the amendment: 

Applicant has amended the claims to remove the unsupported new claim element. Therefore, this rejection is **withdrawn**.

### **NEW CLAIM REJECTIONS**

#### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 4, 6-7, 9-11, 13, 19, 21, 23-24, and 82 are rejected under 35

U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds tested and demonstrating efficacy, does not reasonably provide enablement for the asserted utility of the entirety of the claim scope. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Particularly relevant to the instant case is the issue as to whether the specification provides embodiments allowing use of the claimed invention without requiring undue experimentation by one of ordinary skill in view of the highly unpredictable nature of antibiotic pharmaceutical development.

"[An inventor] must not be permitted to achieve . . . dominance by claims which are insufficiently supported and hence not in compliance with the first paragraph of 35 U.S.C. 112. That paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously

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varies inversely with the degree of unpredictability of the factors involved." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

Accordingly, the critical element here how broad the claims are compared to the level of unpredictability in the art.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Electronics*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

*Nature of Invention.* The nature of the invention involves pharmaceutical compounds for antibiotic use.

*Scope of the Invention.* The scope of the invention is for a genus of compounds of formula I with in excess of billions of species.

*State of the Art and Level of Skill in the Art.* Although the level of skill in the art is very high, antibiotic pharmaceuticals is a very unpredictable art. Barden et al. (J. Med. Chem., 1994, v. 37, no. 20, p. 3205-3211) shows that very slight perturbations in the structure of tetracycline compound (such as changing a methyl group to a methoxy, see Table 1 compounds 9 vs. 12) causes the pharmaceutical to become inactive (see Applicant's Argument, bottom of page "-17-").

*Number of Working Examples and Guidance Provided by Applicant.* The applicant provides table 2 on pages 42-53 showing 69 compounds as having "\*, \*\*, or \*\*\*" levels of activity with approximately 47 of these compounds falling outside the scope of the present claims. Thus, applicant provides data for approximately 22 compounds to support the utility of the scope of the claims.

*Unpredictability of the Art and Amount of Experimentation.* The art of using pharmaceuticals as antibiotics is highly unpredictable as shown by Barden et al. In nearly every case, the skilled artisan could not predict *a priori* whether a given pharmaceutical would act as an antibiotic. At the same time, small variations in structure such as changing methyl to methoxy has radical effects on the activity of a compound. Thus, one of skill in the art would be required to synthesize, purify, characterize, and test each compound within the claim scope to confirm its utility. In addition, without specific guidance or correlations indicating how the structure of

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species affects its ability to act as a antibiotic, the scope of enablement is constrained to compounds showing pharmaceutically predictable variations from those actually demonstrated to be useful. Furthermore, there would be a huge amount of undue experimentation required in order to synthesize and screen the billions of compounds within the claimed scope.

Considering the above factors, the claims are not enabled for the full scope of the compounds claimed. The examiner recommends either amending the claim scope to only those compounds closely resembling the compounds actually tested and disclosed in the specification or provide additional data and/or structural correlations to guide one of ordinary skill in the art to compounds possessing the asserted utility.

***Claim Objections***

5. Claims 32, 103, 109, and 110 are objected to for being dependent on a rejected base claim.

***Conclusion***

The claims are not in condition for allowance.

***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT HAVLIN whose telephone number is (571)272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert Havlin/  
Examiner, Art Unit 1626